Randomised clinical trials in general practice: lessons from a failure

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It is increasingly recognised that there are important advantages in studying problems and testing potential solutions in the setting where such problems are most often met. Advantages include the easier acceptance and transfer of results and the development of a research oriented attitude, which in medicine would be expected to increase the quality of care.[1,2]

Isolated systolic hypertension is a common risk factor for cardiovascular and cerebrovascular events in the elderly population.[3,4] Because of the attention focused on it in the mid-1980s we decided that treatment of this condition would be a good subject for a test randomised trial in the setting of general practice. Care of elderly people forms a large part of general practice, and narrowing the gap between research findings and therapeutic behaviour with respect to hypertension is a priority public health target.[5-7]

Based on the promising experience of a collaborative epidemiological study[8] we planned a randomised controlled trial, which aimed at recruiting a large number of general practitioners on a voluntary basis. We thought that the trial in general practice could produce information confirmatory or complementary to that expected from other large studies then being conducted or planned in clinical settings.[3,9,10]

The main aim of the study was to test the hypothesis that treatment of isolated systolic hypertension in elderly people reduces mortality and morbidity from cardiovascular and cerebrovascular causes. The secondary aim was to evaluate the hypotensive effect and safety of the most widely used hypotensive regimens. However, after the feasibility phase of the study had been completed the study was ended. The reasons for the failure of this trial could offer an insight into the relation between research findings and methods and attitudes and performance in general practice.

The study

Preparation for the study took about 18 months. During this time we tried to establish active collaboration between the general practitioners and the coordinating group; general practitioners were recruited either through an advertisement in a widely read medical journal or from doctors who had already collaborated in studies organised by our institute. We held central and local meetings to discuss each draft of the protocol and written material was distributed periodically. The forms to be used in the study were tested to ensure that their structure was compatible with use in general practice. Much of the discussion with general practitioners was specifically concerned with the acceptability of the rather complex process of recruiting patients (figure).

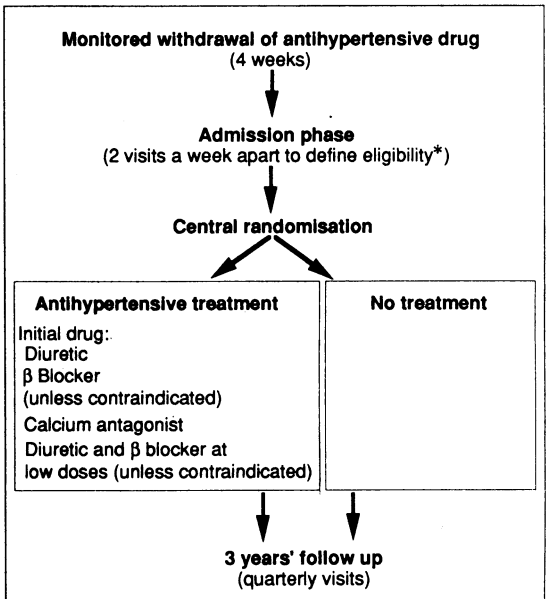
Of 806 general practitioners and five old people's homes who agreed to participate in the study, only 88 general practitioners and two homes eventually started recruitment; 63 general practitioners (7·8% of initial cohort) and two homes actually recruited and followed up at least one patient. Of the 447 patients considered for recruitment, 351 were judged eligible for admission to the trial (each general practitioner recruited on average 4·5 patients while the two old people's homes recruited 38 and 22 patients). Recruitment followed the criteria in the protocol in 338 (96·3%) cases. Eight (1·8%) of the 447 patients refused to enter the recruitment phase and six (1·8%) of the 338 correctly recruited patients refused to enter the trial; few patients (1·2%) dropped out during the first six months' follow up.

Attendance at follow up at three and six months was 94·6% and 93·9% of expected, respectively. During the follow up period no patient was excluded because of general practitioners' unsatisfactory compliance with the study protocol.

Because of the small number of doctors participating in the study and the low rate of recruitment (a goal of at least 3500 randomised patients had been planned) the coordinating group decided to discontinue recruitment.

Comments

We found a large discrepancy between the number of doctors who agreed to participate (806) and the number who started recruiting (63), even though recruiting doctors thought the protocol acceptable and



Design of randomised controlled trial of treatment for isolated systolic hypertension

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practicable. This apparent contradiction leads to several considerations. The steady refusal of most doctors to follow a protocol that they had originally voluntarily accepted and that incorporated their suggestions might indicate that they were not able or prepared to implement the recognised principles and procedures. On the other hand, the high degree of compliance attained by the minority who started recruiting indicates that the design and the technicalities of the protocol were in fact compatible with routine work and that neither the schedule for diagnosis at admission to the trial nor the procedure of stopping ongoing treatment was damaging to the doctor-patient relationship.

The reasons put forward to justify non-participation (the complexity of the protocol and the difficulty of recruiting patients through withdrawal of current treatment) suggest a more basic level of contradiction, directly bearing on the relation between research and delivery of care. The protocol, though complex, was produced after close consultation with general practitioners. Indeed, it simply listed the sequence of procedures recommended as good standard practice to ascertain reliably the presence and degree of hypertension and to initiate treatment. The apparent difference between what should be standard behaviour and what is practised is worrying but not unique. It has been reported for other clinical conditions as a result of various factors and has potentially serious implications for the patients' expected outcome.[11-13] Hypertension deserves some specific comments, because it is not so much a disease to be treated as a risk factor to be controlled in view of its medium and long term consequences.

New cases of hypertension were not easily found as most patients were already receiving treatment. It was therefore often necessary to withdraw current treatment to reassess the diagnosis. This logical procedure became a major stumbling block on its own and was a powerful determinant of the trial outcome. Although the doctors who started recruiting did not seem to encounter difficulties in suggesting drug withdrawal to their patients while the underlying condition was verified, most felt uncomfortable with "shifting their image" in the patients' eyes. The change from the role of confident and reassuring prescriber to an attitude of uncertainty (which attracted consensus in the preparatory meetings) raised instinctive resistance in practice, leading to the withdrawal of the general practitioner rather than the patient's treatment. This is even more impressive in the light of the fact that the diagnosis of isolated systolic hypertension could be considered a model case of uncertainty.

The data collected on the small sample recruited support the complex recruitment procedures as a large fraction of the originally randomised population changed diagnostic category during the trial. For example, 23·2% of subjects randomised to non-treatment had a systolic blood pressure <160 mm Hg at the six month follow up in the absence of any antihypertensive treatment.

Our experience obviously reflects an unsatisfactory attitude among Italian general practitioners, who do not have a long record of controlled research. Other countries have a greater tradition of research in general practice.[14] Nevertheless, in other specialties, contrary to expectations, Italian hospital doctors have shown to be quite successful at recruiting patients in large scale trials comparing new treatment with routine conditions of care.[15 16]

How to increase compliance

If continuity is to be established between research and general practice, it has to be sought within the often conflicting conditions of the health service. Controversies between the Italian health service and the general practitioners' unions arose during the trial, making the atmosphere less than ideal for cultural exercises requiring some degree of commitment. Better compliance might have been obtained through economic incentives. General practitioners were offered only documentation and methodological training opportunities, although financial incentives are forcefully proposed by some doctors' unions. A policy of incentives, however, would contradict the view that formal research into uncertain issues is a challenging component of practice, which is professionally and therefore ethically necessary to meet public health goals.[2 17]

A World Health Organisation European working group recently stressed that general practice, though contributing the most prescriptions, has produced an insignificant fraction of knowledge in the specialties which cannot be investigated outside the ambiguities of clinical practice.[18] The multiplication of descriptive studies of drug use, the successful implementation of observational protocols, and the establishment of networks for health care research are certainly important steps towards a higher profile role for research in general practice.[8 19]

Experimental research must be given priority as a means of gaining a better understanding of the process of increasing knowledge of medicine from within. This is essential if general practitioners are to acquire a truly independent "cultural" status, but it can be attempted only for topics with clear clinical relevance. Clearly, general practitioners did not see isolated systolic hypertension in these terms, possibly because it is not a common problem and possibly because of the intrinsic difficulty of differentiating the condition within the wide diagnosis of hypertension. Questions to be tested must be of concrete daily interest: they are no use if they are merely the products of scientific advertising, however attractive. This is one of the main lessons we have learned as an interdisciplinary group of investigators and general practitioners.

Another equally important step would be to adopt the strategy that has proved successful for hospital based research in general practice.[1 15 16] Truly important questions need only simple protocols and data collection forms, which in fact help general practitioners streamline their office routines. A long term exercise aimed at generating research hypotheses that arouse the natural interest and curiosity of large groups of general practitioners could be the methodological and cultural starting point for efficient controlled trials.

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We don't have a computer

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Six years ago our practice, operating from two separate health centres, decided to become computerised. Now, in 1991, 98% of children are immunised (a 94·6% rate as calculated for target purposes); the cervical cytology rate is 88·4% among women aged 25-65 (excluding those who have had hysterectomies), with a 100% contact and response rate; 99·6% of the names on the practice list coincide with the family health services authority list—a difference of 35 patients in a list of 9800 patients. Moreover, repeat prescribing has virtually been abolished; appointments are at 10 minute intervals, and we operate eight disease registers. Our prescribing costs are 10% below the family health services authority average, and 99% of our case notes are summarised. These achievements are not unique—indeed they are met by many practices—but in our case they have been obtained without a computer.

Computers are generally seen to be an essential part of good modern general practice. In this paper I hope to show that this is not necessarily so; the improvements made in general practice and said to be due to computers have been caused by other factors. The introduction of computers is neither cost effective nor time effective; they should be relegated to research roles in general practice.

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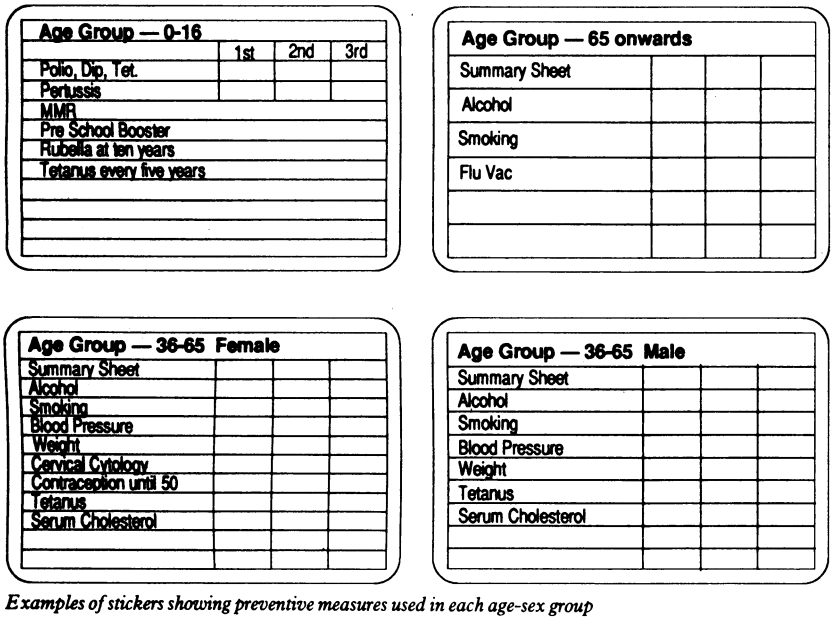
Need for a controlled trial

When we decided to computerise we agreed to organise and summarise all the material to be fed into the computer ("input" material) before buying the machine. Once the computer was installed all the data would be transferred by a secretary. After three years, however, by which time 70% of the records had been summarised and coded, we came to the conclusion that nearly all the reasons for having a computer were no longer valid. We all found that we had improved our manual system so that it could achieve almost all the various functions and tasks that a computer might help with. So we decided to concentrate on organising our manual system more efficiently.

Some 70% of general practitioners have or soon will have a computer, and these practices have all incurred heavy expenditure in terms of money and effort. Furthermore, practices using computers seem to need more staff. Controlled trials do not seem to have been done, yet the introduction of computers should be seen as similar to the introduction of a new drug, and we should at least try to determine whether the disadvantages outweigh the advantages. By chance our practice went through all the steps necessary for computerisation without becoming computerised; and our data provide a basis for a critical assessment of computerisation in the same way as in a comparative drug trial.



Examples of stickers showing preventive measures used in each age-sex group

How the system works

The manual system we use has an updated age-sex register held on cards with patient registration, immunisation, and cervical cytology details. The appointment and visit books give details of consultation rates, etc (including emergency consultations) and are used to provide data for the practice report and statistical review. A record of all visits, including out of hours and repeat visits, is kept by each doctor. The record envelope is the essential cog in the system: each patient's notes contain a coloured sticker for chronic diseases, which acts as the basis for our disease index. Inside the notes is a patient profile and summary-problem list on a separate card, and this is regularly reviewed. This is on an overprinted FP9A or FP9B card. To facilitate this we have separate self adhesive stickers on the back of the notes which indicate to receptionists and doctors at a glance whether the inside profile is up to date and whether the agreed preventive measures are due (see figure). The preventive tasks have been agreed and differ for each age group and also for sex in one age group.

Comparison with computerised practices

I have compared our measurable data with those given in response to a questionnaire by five similar practices in our area that have installed computers (see table). The comparison shows few differences in most